



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
<https://www.wjgnet.com>

Reviewer#1

Specific comments to authors

No.

Reply: Thanks for your comments.

Reviewer#2

Specific comments to authors

The present review discussed the Association between metformin and vitamin B12 deficiency in patients with type 2 diabetes, and advised that people taking metformin undergo annual testing for vitamin B12 deficiency. It is an interesting topic, and the authors provide a new perspective on metformin-related side effects. Major concerns: As the authors focus on the effect of metformin on the absorption of vitamin B12 and on its proposed mechanisms in hindering vitamin B12 absorption, related clinical and experimental evidences are not that solid; The authors did not convince readers whether vitamin B12 supplementation could counteract the metformin-induced complications.

Reply: Thanks for your valuable comment. We tried to consider your comment and added many meta-analyses and randomized control studies that confirmed the relationship between chronic use of metformin and Vitamin B1 deficiency. In addition, we added a new section to our review (Treatment of Metformin-induced Vitamin B12 Deficiency) and we used highly ranked articles and studies in it, so in this way, we could convince the reader better.

Reviewer#3

Specific comments to authors

This review summarizes the relationship between metformin and vitamin B12 in diabetes, the topic selection of the article is very good, however, this is not a new topic in

the field of diabetes, related Review has been published recently, such as (World J Diabetes. 2021 Jul 15; 12(7):916-931), therefore, compared with the published Review, authors should highlight their own highlights in this Review. In addition, a clear picture is necessary to delineate the relationship between metformin and vitamin B12 in diabetes, so that the reader can quickly understand the mechanism. The mechanism of the relationship between metformin and vitamin B12 should be elaborated particular in this review.

Reply: Thank you for your helpful comment, for the first point; actually, our review differs from the review that you have mentioned in many main points we can summarize them as follows:

Our review provided summarized information about the topic based on very valuable studies (interventional studies, observational studies, and meta-analyses) about the relationship between metformin and Vitamin B12 deficiency and this may be so helpful for all clinicians to make a good clinical decision.

Our review focused on the mechanism of decreasing Vitamin B12 absorption by metformin and provided a simplified visual illustration of that.

Our review discussed the possible complications (neurological, psychological, and hematological) accompanied by the metformin-induced Vitamin B12 deficiency in diabetic patients.

Also, we considered your second point and added a simple figure to illustrate the mechanism of the relationship between metformin and vitamin B12.

Revision reviewer

Specific comments to authors

I agree to accept this manuscript without further comment.

Reply: Thanks for your comments.